

Choriocarcinoma in Enugu, South east Nigeria: A Need for a Shift From Mortality to Survival

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ABSTRACT

BACKGROUND: The diagnosis of cancer in Nigeria is often translated to mean an imminent death for the patient. This contrasts the situation in some developed settings where cancer survivorship and its management have evolved. Choriocarcinoma is a rare but curable tumour so; it became necessary to review cases of this curable cancer managed at a tertiary health center in a typical resourced-constrained setting.

METHODS: A retrospective analysis of consecutive choriocarcinoma cases managed at a tertiary hospital in Enugu, South-eastern Nigeria over a five year period. Data analysis was descriptive.

RESULTS: Five non-metastatic and 10 metastatic cases of choriocarcinoma were managed. The mean age of patients was 33.6±9.1 years. All patients had vaginal bleeding with a mean duration of 4±5.19 months. The commonest predisposing factor and metastatic site were abortion (46.7%) and lungs (40.0%) respectively. The mean unit of blood transfusion during treatment was 5.3±3.8 units. Eight patients (53.3%) died on admission while 7 (46.7%) were lost to follow-up during chemotherapy 20.0% or after chemotherapy (26.7%).

CONCLUSION: The case fatality for choriocarcinoma and loss of patients to follow-up in Enugu, Nigeria were high. To shift from this situation of high mortality to that of survival, an improved follow-up of post-abortion patients and aggressive tracing of defaulters are recommended.

KEY WORDS: Choriocarcinoma, mortality, cancer survival, Nigeria

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INTRODUCTION

The diagnosis of cancer in Nigeria is often translated by patients, relatives and caregivers to mean an imminent death for the victim. It is therefore not surprising that discussions on the long-term management of cancer survivors, which has evolved in developed nations,¹ are yet to develop in our environment. Because choriocarcinoma is generally viewed to be curable,² it is believed that a review of cases of this rare tumour managed at a tertiary center in a typical resourced-constrained setting would serve as a platform upon which one reflects on the chances of survival from commoner and “non-curable” tumours in Nigeria and related countries.

Choriocarcinoma is a malignant form of the spectrum of diseases called Gestational trophoblastic diseases (GTD) which is derived from abnormal proliferation of the gestational trophoblast.² The disease spectrum begins with the benign form called hydatidiform mole, through the locally metastatic invasive mole, to the malignant choriocarcinoma and placental site trophoblastic tumour.² Choriocarcinoma is a pure epithelial tumour that metastasizes widely through the blood stream.³ It has also been described as the commonest cancer involving the uterus which metastasizes to the lungs.⁴ Like other types of GTD, choriocarcinoma affects women of reproductive age group at a time when their social and economic commitments are at the peak.⁵ It is associated with pregnancy and may accompany or follow any type of pregnancy including molar pregnancy, term pregnancy, abortions and ectopic pregnancies.⁶ It is commoner in Africa and Asia but rare in European and North American populations.⁷ In Nigeria, it constitutes 21.5% of all cases of GTD;⁸ the second and fourth commonest genital malignancy in Ibadan, South west Nigeria,⁹ and Maiduguri, North east Nigeria respectively.¹⁰ According to the International Federation of Gynecology and Obstetrics (FIGO),¹¹ choriocarcinoma is clinically categorized into four stages thus - Stage I is when the disease is confined to the uterus while stage II disease has spread to genital structure(s); stage III involves metastases to the lungs, while stage IV describes disease that has spread to other sites. Likewise, a modified WHO Prognostic scoring system based on eight risk factors is used to categorize the disease into low or high risk disease, and it has been shown that the high risk disease responds poorly to single agent chemotherapy.¹¹

Choriocarcinoma is an unusual tumour in that it is very chemosensitive and curable in the majority of cases unlike most other malignancies - the low-risk and high-risk types have cure rates of about 100% and 75% respectively.¹² Fortunately, the tumour also elaborates a marker called human chorionic gonadotropin (hCG) which assay in serum or urine is used for diagnosis, treatment monitoring and follow-up.¹³ Nevertheless, despite these favourable characteristics of the disease, its treatment may not be very successful in resourced-constrained settings including Nigeria, hence this study.

MATERIALS AND METHODS

The study was a retrospective analysis of consecutive cases of women managed for choriocarcinoma at the

University of Nigeria Teaching Hospital (UNTH) Enugu, South east, Nigeria over a five year period of 1st January 2002 to 31st December 2006.

A list of cases of choriocarcinoma was made from the admission register at the gynaecological ward of the hospital. The case folders were retrieved from the Records department of the hospital after necessary approvals. Information sought for include patients' age, parity, blood group, clinical features, and outcome of treatment.

Data analysis was descriptive using *Statistical Package for Social Sciences (SPSS) computer software version 13.0 for windows* [SPSS INC: Chicago Illinois]. Study results were presented using simple percentages and tables.

Enugu town is the capital of Enugu state which is one of the five Igbo speaking states in the south east geo-political zone of Nigeria. The state has a land area of about 8000 km² which is located within the West African rain forest region; and has 17 local government areas, most of which are rural.¹⁴ As at the end of the study period, the Enugu state had a population of 3,257,298

with a female to male ratio of about 1:1.¹⁵

The UNTH, Enugu is a government owned tertiary hospital located in the South east geo-political zone of Nigeria. The hospital offers specialist care to the residents of the state and beyond. During the period under review, it was essentially the only health institution within the state equipped with the personnel and some basic support services for the management of choriocarcinoma. Further details of the study area / center have been described in a recent study.¹⁶

RESULTS

There were 15 cases of choriocarcinoma and 3,495 deliveries during the study period which gave a prevalence of 4.3 cases of choriocarcinoma per 1,000 deliveries. Five (33.3%) cases were non-metastatic (FIGO Stage I) while the remaining 10 (66.7%) cases were metastatic. Out of the latter, 3 (30.0%) cases had metastasis to the lungs while another 3 (30.0%) had sub-urethral metastasis. Further details of the FIGO clinical staging of the patients is shown in table 1.

Clinical presentation

The mean age of patients was 33.6 ± 9.1 years (range =

Table 1: Clinical characteristics of patients

Patients variable	Variable sub-groups	No of cases (%)	Dead (%)	Lost to follow-up (%)
FIGO staging	I No metastasis	5 (33.3)	0 (0.0)	5 (100.0)
	II Anterior vaginal wall	1 (6.7)	1 (100.0)	0 (0.0)
	Sub-urethral	3 (20.0)	2 (66.7)	1 (33.3)
	III Lung only	3 (20.0)	3 (100.0)	0 (0.0)
	Lungs and sub-urethral	3 (20.0)	2 (66.7)	1 (33.3)
	IV -	0 (0.0)	0 (0.0)	0 (0.0)
Anaemia category	Mild	2 (13.3)	0 (0.0)	2 (100.0)
	Moderate	6 (40.0)	1 (16.7)	5 (83.3)
	Severe	7 (46.7)	7 (100.0)	0 (0.0)
Size of uterus (cm)	10 - 12	7 (46.7)	3 (42.9)	4 (51.7)
	14 - 16	6 (40.0)	5 (83.3)	1 (16.7)
	18 - 20	2 (13.3)	0 (0.0)	2 (100.0)
Pints of blood transfused	0	2 (13.3)	0 (0.0)	2 (100.0)
	1 - 6	8 (53.3)	4 (50.0)	4 (50.0)
	7 - 12	5 (33.3)	4 (80.0)	1 (20.0)

18-48). The median parity was 1 (range: = 0-6). Details of the patients' socio-demographic characteristics are shown in table 2.

Table 2: Distribution of patients' socio-demographic characteristics

Patients variables	Variable sub-groups	Frequency (%)
Age groups (years)	20 or less	2 (13.3)
	21 - 30	3 (20.0)
	31 - 40	7 (46.7)
	41 - 50	3 (20.0)
Age range (years)	< 40	11 (73.3)
	>= 40	4 (26.7)
Marital status	Married	13 (86.7)
	Single	2 (13.3)
Parity groups	>= 5	4 (26.7)
	2 - 4	3 (20.0)
	1	6 (40.0)
	0	2 (13.3)

All the patients presented with complaint of vaginal bleeding of varying duration with an average of 4 ± 5.19 months (range = 1 - 18). The condition was preceded by term pregnancy in 4 patients (26.7%), abortion in 7 patients (46.7%), and molar pregnancy in the remaining 4 patients (26.7%). The interval between antecedent pregnancy and diagnosis of the condition was 1-6 months in 8 patients (53.3%), 7 - 12 months in 1 patient (6.8%), and 1-2 years in 6 patients (40.0%). All the patients were anaemic on admission with majority (46.7%) of them having severe anaemia. The median packed cell volume (PCV) on admission was 21.0% (mean = $21.2 \pm 6.0\%$, range = 7 - 31). All patients had uterine enlargement of varying degree with a median uterine size of 14 weeks (range = 10-20). Details of the distribution of patients according to anaemia and uterine size categories are shown in table 1.

Investigations

Urine pregnancy test (neat, and in dilution), abdominopelvic ultrasonography, chest radiography, full blood count, blood grouping, liver function test, and renal function test were done for all patients. Histological confirmation of diagnosis was carried out in 6 patients (40.0%), while elevated urine hCG were used for diagnosis in the remaining 9 patients (60.0%). Eleven patients (73.3%) belonged to blood group O Rhesus D positive (O^{+ve}), 2 (13.3%) were B^{+ve} , while blood groups A^{+ve} and AB^{+ve} had one patient (6.7%) each. None of the patients had Rh D negative blood group.

Treatment

All patients were admitted into the gynaecology ward during evaluation and treatment. The mean duration of admission was 63.8 ± 32.9 days (range = 20-120). A majority (86.7%) of the patients received transfusion of typed and screened blood depending on their state of anaemia. In all, eighty units of blood were transfused to these patients and the median units of blood transfused per patient was 5 (mean = 5.3 ± 3.8 units, range = 0 - 12). Chemotherapy was initiated for all patients following diagnosis. Three patients (20.0%) received monotherapy of methotrexate only, 11 (73.3%) received combination therapy of methotrexate, actinomycin-D, and cyclophosphamide, while 1 patient (6.7%) received combination therapy of cisplatin and vincristin.

Outcome

Eight patients (53.3%) died in the ward after a median cumulative duration of admission of 66.9 days (mean = 65.5 ± 39.7 days, range = 20-120). The cause of death in each case was haemorrhagic shock from uterine bleeding. The remaining 7 patients (46.7%) were lost to follow-up either in between courses of chemotherapy (3 patients) or after completing their courses of chemotherapy (4 patients). Details are contained in table 3.

Table 3: Case fatality of choriocarcinoma in Enugu, Nigeria

Tumour characteristics	Completed treatment (%)	Incomplete treatment (%)		Case fatality (%)	
		Defaulted	Died on admission	Best scenario	Likely scenario*
Non-metastatic (n = 5)	4 (80.0)	1 (10.0)	0 (0.0)	0.0	20.0
Metastatic (n = 10)	0 (0.0)	2 (20.0)	8 (80.0)	80.0	100.0
Total (n = 15)	4 (26.7)	3 (20.0)	8 (53.3)	53.3	73.3

*: Assume all defaulted patients died

DISCUSSION

The mean age for the occurrence of choriocarcinoma of 33.6 years was similar to 30.6 years reported from Port-Harcourt South-southern Nigeria.¹⁷ It has been documented that incidence of choriocarcinoma increased with age and was 5-15 times higher in women aged 40 years and above when compared to younger women.¹⁸ However, the reverse was almost the case in this study where the prevalence of the disease was about 3 times higher in women less than 40 years when compared to older women (table 2). Furthermore, this study shows that the disorder was commoner in the 4th

decade of life as against the 3rd decade of life reported from Northern Nigeria.¹⁹ This difference in reported peak age may be related to the fact that women in southern Nigeria tend to marry later than their counterparts in the Northern part of the country.

Furthermore, unlike the study from Benin Nigeria which found that most cases of choriocarcinoma were preceded by normal pregnancy,²⁰ our study showed that the commonest predisposition to choriocarcinoma was abortion while the least was molar pregnancy. Likewise, these findings did not conform to the usual teaching that hydatidiform mole was the antecedent pregnancy in up to 50% of cases of choriocarcinoma.^{3,6} However, in the absence of histological examination of abortuses, it is possible that some cases reported as abortion by patients in this study could have been molar pregnancies.¹¹ On the other hand, it is equally likely that the traditional teaching on the antecedent pregnancy to choriocarcinoma, may not represent the true situation in Nigeria. Therefore, considering the small sample size in this study, a large scaled multi-center prospective study on choriocarcinoma is highly necessary to generate the true epidemiology of the disorder in our environment.

Urine pregnancy test was used for diagnosis and follow-up in the study because the more sensitive assay for serum B-hCG was not available in the center. This situation may not be different for some other referral centers in Nigeria. For instance, a case report from Northern Nigeria used urine pregnancy test in the management of metastatic choriocarcinoma.²¹ Also, another report on GTD from Ilorin, Nigeria noted that urine pregnancy test in dilution was used for patient diagnosis and follow-up because the facility for quantitative B-hCG assay was lacking.²² Nevertheless, though serum B-hCG is the gold standard for diagnosis and follow-up of malignant GTD, concurrent use of urine and serum hCG assay has been recommended so as to rule out false positivity inherent with serum hCG which is due to the presence of heterophilic antibodies in some individuals.²³

Interestingly, none of the women identified in the study had a rhesus negative blood and our extensive literature search did not reveal a report of GTD in a rhesus negative woman. This raises the possibility that rhesus negativity may be protective against the disease and calls for further study. As expected, the commonest metastatic site was the lungs however; it is interesting to note that sub-urethral metastasis was equally common in this study it is therefore important that specialist involved in choriocarcinoma case management should specifically examine for the metastasis because it is a common site of blood loss.

The haemorrhagic nature of the illness was supported by

our finding that all patients were anaemic at presentation with an average blood transfusion per patient of 5 units. It is therefore obvious that the management of choriocarcinoma should be carried out in a specialist center with functional blood banking services. The study also suggests a trend where patients that were severely anaemic on presentation were likely to die while those with mild or moderate degrees anaemia were likely to default from treatment (table 1). It therefore calls for a more aggressive management of severely anaemic cases so as to reduce mortality; as well as a scaled-up in the counselling and monitoring of mild to moderate anaemic cases to minimize default from follow up.

The case fatality of 53.3% in this study is very high and is not in line with the global view that choriocarcinoma is curable in 75 - 100% of cases depending on the severity of the disease.¹² Also, it is likely that the 3 patients lost to follow-up during chemotherapy died, which would increase the case fatality to 73.3%. This finding may not be surprising because an earlier report from Enugu, Nigeria had shown that choriocarcinoma was the second leading cause of gynaecologic mortality.²⁴ Furthermore, it has been noted that the marked improvement in the outcome of treatment of choriocarcinoma was due to a combination of three factors thus: earlier case diagnosis, the ability to precisely measure hCG, and the availability of effective chemotherapy.¹¹ Unfortunately, these conditions are still not optimally developed in the study area so, late presentation and diagnoses of cases as well as sub-optimal management were possible contributors to the high case fatality recorded in this study. The situation is worsened by the cost of choriocarcinoma treatment especially the direct cost of long hospital stay, multiple blood transfusion, and chemotherapy which may be related to the magnitude of loss to follow-up identified in this study.

This study was limited by its retrospective nature and the attendant reliance on case notes. Also, the defaulters from treatment and follow up obviously affected the assessment of the true case fatality. Nevertheless, the study is the first documented analysis on choriocarcinoma from the study area and has identified areas of interest that may stimulate further research in the subject. Prospective studies coupled with an aggressive tracing of defaulters, with a view to encouraging compliance and identifying reasons for defaulting, are highly encouraged.

In conclusion, deaths due to choriocarcinoma and loss of cases to follow-up in Enugu, South-eastern Nigeria were high within the period reviewed, and the current situation might not be different considering the worsening health care system and poverty in Nigeria. To shift from the situation of high mortality to that of

survival, which is the expected trend in cancer management, an improved follow-up of post-abortion patients, review of local management protocols, aggressive tracing of defaulters are recommended. Most importantly, because of the high financial cost of choriocarcinoma treatment, free or subsidized treatment by government / non-governmental agencies will improve patients' compliance and reduce loss to follow-up. Furthermore, in the spirit of "Global Partnership for Development" being propagated by the United Nations' Millennium Development Goals initiative, it is hoped that established gynaecologic oncology centers in high resource countries should assist training institutions in under-resourced countries to develop effective and sustainable gynaecologic oncology services.

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